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13. ABSTRACT *(Maximum 200 Words)*

The goal of this training program is to dramatically extend our existing, highly successful Interdisciplinary Doctoral Training Program in Tumor Biology with a new track which integrates genetics, molecular epidemiology, and prevention of breast cancer. This new track offers both MD/PhD and PhD training opportunities, and integrates new faculty from the Lombardi Cancer Center Programs in Cancer Prevention and Control, and Cancer Genetics. The program is enriched by new courses, as well as practical research experience. This new programmatic initiative makes use of the existing organizational structure of the Interdisciplinary Doctoral Training Program in Tumor Biology and incorporates a multi-disciplinary faculty who are devoted to research and education in breast cancer. We have successfully completed our second year of the program and recruited our third incoming class of 2 MDs who are interested in pursuing PhDs. In addition, 1 MD/PhD student and 1 PhD student are continuing into their second year of enrollment in the program. Finally, new courses in Genetics in Health and Society and Biostatistics have been added to the program.

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FOREWORD

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Robert B. [illegible] 1/30/01

PI - Signature Date

COMBINED MD/PHD AND PHD TRAINING PROGRAM IN BREAST CANCER PREVENTION

TABLE OF CONTENTS

COMPREHENSIVE POSTDOCTORAL TRAINING PROGRAM IN BREAST CANCER BIOLOGY

INTRODUCTION

The goal of this program is to dramatically extend our existing, highly successful Interdisciplinary Doctoral Training Program in Tumor Biology with a new track which integrates genetics, molecular epidemiology, and prevention of breast cancer. This new track offers both MD/PhD and PhD training opportunities, and integrates new faculty from the Lombardi Cancer Center Programs in Cancer Prevention and Control, and Cancer Genetics. The program is enriched by new courses covering cancer genetics, molecular epidemiology, and cancer prevention, as well as practical research experience. This new programmatic initiative makes use of the existing organizational structure of the Interdisciplinary Doctoral Training Program in Tumor Biology and incorporates a multi-disciplinary faculty who are devoted to research and education in breast cancer.

BODY

Training and Research Accomplishments

The accomplishments of this new program in its second year fall into two categories: the recruitment and progress of new trainees, and the development of courses for the program. In terms of recruitment, the third incoming class of this new track in the Interdisciplinary Doctoral Training Program in Tumor Biology consists of two who are PhD candidates, Ion Cotarla, M.D. and Riddish Shaw, M.D., each of whom have one year advanced standing in terms of prior graduate coursework. Both of these candidates were selected based on their outstanding qualifications and the compatibility of their interests with the goals of this program. Both application statements expressed an interest in both breast cancer and cancer prevention, and Dr. Cotarla indicated that he wishes to build on his breast cancer research experience obtained while working with Dr. Priscilla Furth at the University of Maryland. Both trainees will perform additional laboratory rotations in order to select a thesis research laboratory, and both are now completing course requirements.

Three trainees had been recruited for the second incoming class of the Breast Cancer Prevention Track of the Interdisciplinary Doctoral Training Program in Tumor Biology: one MD/PhD candidate, Ms. Carolyn Lee, and two PhD candidates, Ms. Sonia DeAssis and Mr. Elijah Herbert. Ms. DeAssis has a master's degree and research experience in the field of breast cancer, and is interested in breast cancer prevention as related to diet and environment. She has successfully completed her first year of training and is now starting her second year in this program. Ms. Lee is interested in cancer genetics and breast cancer, and has joined Dr. Todd Waldman for her thesis research. Unfortunately, Mr. Elijah Herbert withdrew from the program after only a few months

for very acute health reasons; we were able to use his slot in the program for recruitment of Ms. Carolyn Lee (above).

Two trainees had been recruited into the first incoming class, Ms. Christine Cottichia and Ms. Stacey Kessler. Ms. Cottichia had a very successful year. She has received a DOD predoctoral fellowship, she passed her comprehensive examination and she will proceed with thesis research with Dr. Robert Dickson. Unfortunately, Ms. Kessler withdrew from the program for personal reasons, but she earned a Masters degree in Tumor Biology.

In the review of our prior funding period, reviewers noted the desirability of accelerating the recruitment of MD/PhD candidates to the program. As described above, we now have three such candidates (a majority) out of the overall five students for our new program. We expect this trend to continue. A number of MD/PhD candidates have specifically stated an interest in the program for their PhD training. Ms. Aparna Mani, an MD/PhD student, is performing rotations exclusively in Tumor Biology laboratories and is expected to join the program next year.

In addition to the existing core course work of the Interdisciplinary Doctoral Training Program in Tumor Biology, new course components have been incorporated into the Breast Cancer Prevention track. These include a new course in *Biostatistics, Applied Biostatistics,* that has been refocused on statistical design and methodology for research rather than biostatistics theory, and a *Cancer Genetics* course, *Genetics, Health, and Society in the 21st Century* course, which focuses on practical and ethical questions raised by genetic information and technology. Both courses will be offered in the Spring 2002.

Topics in Molecular Epidemiology of Cancer Risk was introduced last year by Dr. Peter Shields, and is offered in both the Fall and Spring semesters. This course focuses on the latest developments in the field of cancer risk assessment and explores how interindividual variation contributes to cancer risk. Topics ranging from epidemiology to cancer genetics for carcinogen metabolism, DNA repair, signal transduction and cell cycle control, as well as methods for developing new biomarkers and quality control are covered.

Principles of Cancer Prevention, has had a successful first year. It covered the general principles of cancer prevention by life-style modifications from the basic science, clinical, and epidemiologic perspectives, with special emphasis on nutrition, environment and specific behaviors.

All of these courses emphasize breast cancer, as most of the teaching faculty are extensively involved in breast cancer research. Interest in these courses has not been limited to students in the new Breast Cancer Prevention track: a number of additional students in the Interdisciplinary Doctoral Training Program in Tumor Biology and other biomedical graduate programs at Georgetown University have enrolled as well.

KEY ACCOMPLISHMENTS

- *Recruitment of New Trainees and Advancement of Existing Trainees:* Two PhD candidates, Ion Cotarla, M.D., and Riddish Shaw, M.D. One MD/PhD candidate, Ms. Carolyn Lee and one PhD candidate, Ms. Sonia DeAssis in class #2, continued successfully into the second year of the program. From class #1, one PhD candidate, Ms. Christina Cottichia, successfully completed her comprehensive examination and moved into the thesis phase of her program, while one candidate, Ms. Stacey Kessler received a Masters degree in Tumor Biology.

- *Development of Courses:* The following courses were revised or developed for the Breast Cancer Prevention track of the Interdisciplinary Doctoral Training Program in Tumor Biology – *Biostatistics and Experimental Design, Cancer Genetics, Topics in Molecular Epidemiolory of Cancer Risk, and Principles of Cancer Prevention.* In addition, new courses *Genetics, Health and Society in the 21st Century,* and *Applied Biostatistics* have been added to the program.

REPORTABLE OUTCOMES

- *Publications:*
  - **Carolyn Lee:**
    Berger, C.L., Xu, A.-L., Hanlon, D., Lee, C., Schechner, J., Glusac, E., Christensen, I., Snyder, E., Holloway, V., Tigelaar, R., Edelson, R.L. Induction of human tumor-loaded dendritic cells. *Int J Cancer* 91: 438-47, 2001

  - **Christine Cottichia:**
    Dickson, Robert, Ph.D. Ramljak, D., Coticchia, C.M., Nishanian, T.G., Conzen, S.D., Dickson, R.B. Epidermal growth factor receptor (EGFR) signaling inhibits c-Myc-induced apoptosis through activation of Akt, Erk and upregulation of Bcl-xL in mouse mammary carcinoma cells. (submitted)

    Harris, V.K., Kagan, B.K., Ray, R., Coticchia, C.M., Liaudet-Coopman, E.D.E., Wellstein, A., Riegel, A.T. Serum induction of the fibroblast growth factor-binding protein (FGF-BP) is mediated through ERK and p38 MAP kinase activation and C/EBP-regulated transcription. *Oncogene* (in press)

    Harris, V.K., Coticchia, C.M., List, H.J., Wellstein, A., and Riegel, A.T. Mitogen induced expression of the FGF-binding protein is transcriptionally repressed through a non-canonical E-box element. *J Biol Chem* 275:28539-48, 2000

    Harris, V.K., Coticchia C.M., Kagan, B.L., Ahmad, S., Wellstein, A., and Riegel, A.S. Induction of the angiogenic modulator fibroblast growth factor-binding protein by epidermal growth factor is mediated through both MEK/ERK and p38 signal transduction pathways. *J Biol Chem* 275: 10802-10811, 2000

- *Student Abstracts/Presentations:*

- **Christine Cottichia:**
  Kagan, B.L., Harris, V.K., Coticchia, C.M., Ray, R., Wellstein, A., Riegel, A.T. Transcriptional regulation of a binding protein for FGF (FGF-BP) through p38/SAPK2 signaling. American Association for Cancer Research 92nd Annual Meeting, New Orleans, LA, 2001

  Ramljak, D., Coticchia, C.M., Dickson, R.B. Epidermal growth factor receptor signaling inhibits c-Myc-induced apoptosis through activation of Akt, Erk and up-regulation of Bcl-xL in mouse mammary carcinoma cells. Keystone Symposia on Molecular Mechanisms of Apoptosis, Keystone, CO, 2001

  Coticchia, C., Harris, V.K., Wellstein, A., and Riegel, A. The angiogenic modulator FGF-binding protein (FGF-BP) is transcriptionally regulated by EGF and TPA through the MEK/ERK and p38 signal transduction pathways. Proc of the American Associate for Cancer Research Annual Meeting, San Francisco, 2000

- **Sonia DeAssis:**
  Hilakivi-Clarke, L.A., de Assis, S., Olivo, S., Kerr, L.R., Patterson, E., Gustafsson, J.-A., Cabanes, A. Prepubertal exposure to a high N-6 polyunsaturated fatty acid (PUFA) diet and mammary tumorigenesis in rats. American Association for Cancer Research 92nd Annual Meeting, New Orleans, LA, 2001

  Cabanes, A., de Assis, S., Gustafasson, J-A., Helferich, W., Hilakivi-Clarke, L. Soy intake prevents pregnancy-induced promotion of mammary tumorigenesis in rats. Proceeding of the American Association for Cancer Research 92nd Annual Meeting, New Orleans, LA, 2001

  Cabanes, A., Olivo, S., DeAssis, S., Gustafasson, J-A., and Hilakivi-Clarke, L. Prepubertal exposure to estradiol reduces DMBA-induced mammary tumorigenesis and increases mammary ER-B levels. American Association for Cancer Research 91st Annual Meeting, San Francisco, CA, 2000

- *Awards and Accomplishments:*
  - **Christine Cottichia:**
    Dickson, Robert DOD Predoctoral Fellowship - 7/2001
    The Fas/FasL System in c-Myc-Expressing Mammary Carcinoma Cells

  - **Kessler, Stacey:**
    DOD Predoctoral Fellowship - 7/2001
    3rd Annual Lombardi Cancer Center Research Fair – 2/2001
    1st Place Award (shared) Predoctoral Division

  - **Carolyn Lee:**
    Umeko Strauss Scholar – 2001 (Ms. Lee's tuition and fees are paid by DOD predoctoral program).

- *Stacey Kessler- M.S. in Tumor Biology 2001*

CONCLUSIONS

The goal of this training program is to dramatically extend our existing, highly successful

Interdisciplinary Doctoral Training Program in Tumor Biology with a new track which integrates genetics, molecular epidemiology, and prevention of breast cancer. We have completed our first incoming class a PhD student and have recruited a third year incoming class of two MDs wishing to gain PhDs in breast cancer research. Additionally, new course components have been incorporated into the Breast Cancer Prevention track that focus on cancer genetics, cancer prevention, and epidemiology and cancer risk.